AMENDMENTS TO THE CLAIMS

Please amend claims 3 and 8 and add claims 21 and 22 as set out below. This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A method for the identification/isolation of modulators of a secretase activity wherein

suitable eukaryotic host cells are contacted with a test substance wherein said suitable host cells comprise:

a) a fusion protein comprising a secretory protein, a membrane anchor domain and a secretase cleavage sequence,

b) a protein comprising a secretase activity recognizing said cleavage sequence of said fusion protein and

c) at least one reporter gene under control of a transcriptional activation system wherein said transcriptional activation system is regulated by the release of said secrretory protein from said fusion protein by said secretase activity and its subsequent secretion

then culturing said cells under suitable conditions such tat said reporter gene allowing detection and/or survival of cells is only expressed or repressed in a manner that is dependent on an altered secretase activity due to said test substance.

2. (Original) Method for the isolation of a secretase inhibitor according to claim 1, wherein a reduced or no release of said secretory protein due to a reduced/inhibited secretase activity leads to expression of said at least one reporter gene thereby allowing detection and/or survival of cells under suitable culturting conditions.

3. (Currently amended) Method according to claim 1, wherein said at least one reporter gene is selected from genes conferring antibiotic resistance, genes encoding reporter molecules with an activity that can be detected by colorimetric or fluorescent methods and genes complementing auxotrophies~~, preferably a His3 gene~~.

4. (Original) Method for the identification of agonists of a secretase activity according to claim 1, wherein the release of said secretory protein due to an enhanced

secretase activity leads to a reduced expression of said at least one reporter gene thereby allowing detection and/or survival of cells under suitable conditions.

5. (Original) Method according to claim 4, wherein said at least one reporter gene is selected from genes conferring sensitivity to a chemical.

6. (Previously presented) Method according to claim 1, wherein said cells comprise a second reporter gene selected from the group consisting of:

a) genes encoding reporter molecules with an activity that can be detected by colorimetric or fluorescent methods,

b) genes conferring antibiotic resistance and genes conferring sensitivity to a chemical and

c) genes complementing auxotrophies.

7. (Previously presented) Method according to claim 1, wherein said cell is a yeast cell.

8. (Currently amended) Method according to claim 1, wherein said secretory protein has an enzymatic activity~~, preferably a protein with invertase activity or functional fragments of a protein with invertase activity~~.

9. (Previously presented) Method according to claim 1, wherein said secretory protein is a yeast invertase or functional fragments or a yeast invertase.

10. (Previously presented) Method according to claim 1, wherein said secretase cleavage sequence is selected from the β site and the α site of the human amyloid precursor protein and the S2 site of Notch 1 protein.

11. (Original) Method according to claim 10, wherein into said β site the Lys595Asn and Met596Leu changes were introduced.

12. (Previously presented) Method according to claim 1, wherein said fusion protein comprises an ER retention signal.

13. (Previously presented) Method according to claim 1, wherein said fusion protein comprises amino acid residues 1-532 of yeast invertase, amino acid residues 590-695 of human APP and an ER retention signal.

14. (Previously presented) Method according to claim 1, wherein said fusion protein comprises amino acid residues 1-532 of yeast invertase, amino acid residues 1714-1876 of human Notch 1 and an ER retention signal.

15. (Previously presented) Method according to claim 1, wherein a nucleic acid construct encoding said fusion protein is integrated into the genome of said host cell.

16. (Previously presented) Method according to claim 1, wherein said protein comprising a secretase activity recognizing said cleavage sequence of said fusion protein further comprises an ER signal sequence.

17. (Previously presented) Method according to claim 1, wherein said secretase activity is selected from β-secretase and α-secretase.

18. (Original) Method according to claim 16, wherein said protein comprising a β-secretase activity further comprises an ER signal sequence and amino acid residues 616-695 of human APP.

19. (Previously presented) Method according to claim 1, wherein said transcriptional activation system comprises at least part of the yeast GAL gene regulatory system.

20. (Previously presented) Method according to claim 1, wherein said reporter gene is under control of the yeast GAL1-10 regulatory region.

21. (New) Method according to claim 3 wherein said reporter gene is a His 3 gene.

22. (New) Method according to claim 8 wherein the protein has invertase activity or comprises functional fragments of a protein with invertase activity.